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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/828,995	04/09/2001	Catherine A. McCall	AL-7	9579

26949 7590 04/21/2003

HESKA CORPORATION
INTELLECTUAL PROPERTY DEPT.
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EXAMINER	
SPECTOR, LORRAINE	
ART UNIT	PAPER NUMBER
1647	18

DATE MAILED: 04/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 1/28/03

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 60-80 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☒ Claim(s) 63 is/are allowed.
☒ Claim(s) 60, 64, 66-70, 72-75, 78-80 is/are rejected.
☒ Claim(s) 61, 62, 65, 71, 76, 77 is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

–SEE OFFICE ACTION ON THE FOLLOWING PAGES–

★ U.S. GPO: 1998-404-498/40517

Part III: Detailed Office Action

Newly submitted claims 60-80 are pending.

Formal Matters:

The new title of the invention is acknowledged.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 75-79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 75 is indefinite as it is not clear whether "a canine IL-13Rα2 protein domain" is intended to indicate that the entire IL-13Rα2 *is* a domain of the fusion protein, or alternatively that only one (of several) domains of IL-13Rα2 is present in the fusion protein. Claim 75 is also indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim says only that part (b) encodes a canine IL-13Rα2 protein domain, without any structural limitations. The specification as filed discloses two proteins, designated IL-13Rα1 and IL-13Rα2. Although the two presumably have different sequences and properties, the specification does not provide an adequate written description of the identifying features of the two, i.e. what would make a protein an IL-13Rα1 and not an IL-13Rα2, or vice versa, or even features that would distingish either from other proteins. Thus, the metes and bounds of claim 75 cannot be determined, as the protein is referred to only by name, and as the specification fails to breath life and meaning into that name.

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 60, 64, 66-70, 72-75 and 78-80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids disclosed as SEQ ID NO: 54, 56, 57, 59, 60, 62-65, 67, 68 or 70 or fragments thereof (of specific lengths) or species which vary by codon degeneracy therefrom, as well as with proteins encoded thereby or fragments of said proteins that retain binding function or can be used to make antibodies reactive with said proteins, does not reasonably provide enablement for any nucleic acid comprising nucleic acids only 95% identical to a 60 nucleotide fragment of any of SEQ ID NOs: 54, 56, 57, 59, 60, 62-65, 67, 68 or 70 and which encode a protein that binds a canine IL-13 protein (as in claim 60), nor a nucleic acid comprising as little as 40 nucleotides of SEQ ID NO: 55, 58, 61, 66 or 69 which encodes a protein that binds a canine-IL-13 (as in claim 66), nor any and all possible canine-IL-13Rα2 protein domains (as in claim 75). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The newly introduced claims contain functional limitations regarding the protein. However it remains that enablement is not commensurate in scope with the claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). In this case, the nature of the invention is that applicants have discovered the canid IL-13 receptor alpha subunit. It is noted that applicants have apparently discovered two such subunits, and that it is the α2 subunit which is under consideration. The state of the art is that the human and murine forms of the protein were previously known, see U.S. Patent Number 5,710,023, cited by applicants. Although the

relative skill in the art of recombinant DNA technology is high, little is known about the structure: function relationship for the particularly disclosed proteins, and the art of altering proteins is an uncertain one. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex, as set forth in the previous Office action. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although there exist art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity, as set forth in the previous Office action. In this case, the specification does not disclose which portion of the protein is required for binding activity, nor is it credible that there exists *any* portion of 30 or 40 amino acids (encoded by as little as 60 nucleotides) that would possess such activity. Further, with respect to SEQ ID NOs: 54 and 57, as they only overlap for 44 nucleotides, it is improbable, if not impossible, that there could exist fragments of both that would encode proteins with binding activity. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue

experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope, as that scope encompasses proteins that bind IL-13 or nucleic acids encoding such.

With respect to claim 75, which has no structural or functional requirements but merely requires "a canine-IL-13Rα2 protein domain", the specification does not teach how to make a commensurate number of species, and the written description does not support such breadth, and enablement is not commensurate in scope with claims to any and all possible such domains. The Examiner's position is supported by the decision in *Ex parte Maizel* (27 USPQ2d 1662 at 1665) that:

> Appellants have not chosen to claim the DNA by what it is but, rather, by what it does, i.e., encoding either a protein exhibiting certain characteristics, *or* a biologically functional equivalent thereof. Appellants' claims might be analogized to a single means claim of the type disparaged by the Court of Customs and Patent Appeals in *In re Hyatt,* 708F.2d 712, 218 USPQ 195 (Fed. Cir. 1983). The problem with the phrase "biologically functional equivalent thereof" is that it covers any conceivable means, i.e., cell or DNA, which achieves the stated biological result while the specification discloses, at most, only a specific DNA segment known to the inventor. Clearly the disclosure is not commensurate in scope with the claims."

In this case, applicants have disclosed a single protein that binds IL-13, and are claiming fusion proteins comprising any and all possible proteins that could be described as "a canine-IL-13Rα2 protein domain", which encompasses all functionally equivalent molecules. Clearly, enablement is not commensurate in scope with such a claim.

With respect to claims 78-79, such are drawn to therapeutic compositions of nucleic acids. The art of gene therapy in general, and in dogs in particular, is not considered to be routine or predictable in the art.

Numerous factors complicate somatic cell gene therapy with respect to predictably achieving levels and duration of gene expression, factors which have <u>not</u> been shown to be overcome by routine experimentation. See Eck & Wilson ('Gene-Based Therapy' in The Pharmacological Basis of Therapeutics, 1996), These factors include, the fate of the DNA vector itself (volume distribution, rate of clearance into the tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA

produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced. See page 82, column 1, first paragraph. These factors differ dramatically based on the vector used, the route of administration of the vector, the protein being produced, which cells are the target cells, and the disease and/or host being treated. It is further noted that Eck and Wilson support the importance of tailoring a gene therapy vector and method to specific diseases and/or disorders. See page 82, column 1, first paragraph. For example, Eck & Wilson et al. review the state of the art for gene therapy for inherited disorders and discloses that "[t]he level of protein function necessary to achieve complementation of the defect varies widely among genetic diseases." See page 78, column 2, 2nd paragraph. Accordingly, given that the state of the art indicates unpredictablity and a low level of skill in the art of gene thereapy, and in the absence of any specific guidance as to vectors to be used, and in the absence of any working examples, claims 78-79 are not enabled.

Advisory Information:

Claim 63 is allowable.

Claims 61, 62, 65, 71, 76 and 77 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be

calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

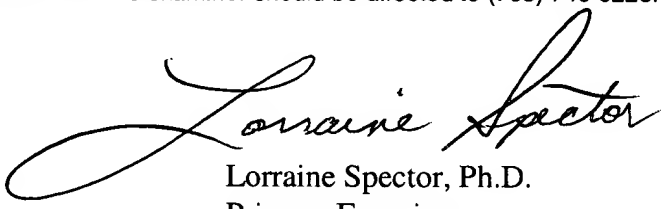
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228.



Lorraine Spector, Ph.D.
Primary Examiner

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4/17/03